

Exhibit A

Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/691,343

4. (Original) An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP gene described in SEQ ID NO:6.

5. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

- (a) encodes the amino acid sequence shown in SEQ ID NO:7; and
- (b) hybridizes to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. (Original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:7.

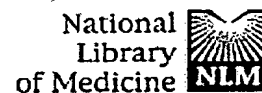
7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

9. (Previously Presented) The isolated nucleic acid molecule of claim 4, comprising the nucleic acid sequence of SEQ ID NO:6.

10. (Previously Presented) The recombinant expression vector of claim 7, wherein said nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:7.

11. (Previously Presented) The recombinant expression vector of claim 10, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:6.



PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bc

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1: Nat Cell Biol 2000 May;2(5):302-9

Related Articles, Link

nature
cell biology**PDGF-C is a new protease-activated ligand for the PDGF alpha-receptor.****Li X, Ponten A, Aase K, Karlsson L, Abramsson A, Uutela M, Backstrom G, Hellstrom M, Bostrom H, Li H, Soriano P, Betsholtz C, Heldin CH, Alitalo K, Ostman A, Eriksson U.**

Ludwig Institute for Cancer Research, Stockholm, Sweden.

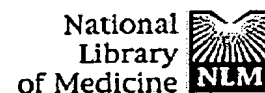
Platelet-derived growth factors (PDGFs) are important in many types of mesenchymal cell. Here we identify a new PDGF, PDGF-C, which binds to and activates the PDGF alpha-receptor. PDGF-C is activated by proteolysis and induces proliferation of fibroblasts when overexpressed in transgenic mice. In situ hybridization analysis in the murine embryonic kidney shows preferential expression of PDGF-C messenger RNA in the metanephric mesenchyme during epithelial conversion. Analysis of kidneys lacking the PDGF alpha-receptor shows selective loss of mesenchymal cells adjacent to sites of expression of PDGF-C mRNA; this is not found in kidneys from animals lacking PDGF-A or both PDGF-A and PDGF-B, indicating that PDGF-C may have a unique function.

PMID: 10806482 [PubMed - indexed for MEDLINE]

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1: J Biol Chem 2001 Jul 20;276(29):27406-14

Related Articles, Link

FREE full text article at
www.jbc.org**Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor.****Gilbertson DG, Duff ME, West JW, Kelly JD, Sheppard PO, Hofstrand PD, Gao Z, Shoemaker K, Bukowski TR, Moore M, Feldhaus AL, Humes JM, Palmer TE, Hart CE.**

ZymoGenetics Inc., Seattle, Washington 98102, USA. gilbertd@zgi.com

We have characterized platelet-derived growth factor (PDGF) C, a novel growth factor belonging to the PDGF family. PDGF-C is a multidomain protein with the N-terminal region homologous to the extracellular CUB domain of neuropilin-1, and the C-terminal region consists of a growth factor domain (GFD) with homology to vascular endothelial growth factor (25%) and PDGF A-chain (23%). A serum-sensitive cleavage site between the two domains allows release of the GFD from the CUB domain. Competition binding and immunoprecipitation studies on cells bearing both PDGF alpha and beta receptors reveal a high affinity binding of recombinant GFD (PDGF-CC) to PDGF receptor-alpha homodimers and PDGF receptor-alpha/beta heterodimers. PDGF-CC exhibits greater mitogenic potency than PDGF-AA and comparable or greater mitogenic activity than PDGF-AB and PDGF-BB on several mesenchymal cell types. Analysis of PDGF-CC in vivo in a diabetic mouse model of delayed wound healing showed that PDGF-CC significantly enhanced repair of a full-thickness skin excision. Together, these studies describe a third member of the PDGF family (PDGF-C) as a potent mitogen for cells of mesenchymal origin in in vitro and in vivo systems with a binding pattern similar to PDGF-AB.

PMID: 11297552 [PubMed - indexed for MEDLINE]

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Abstract

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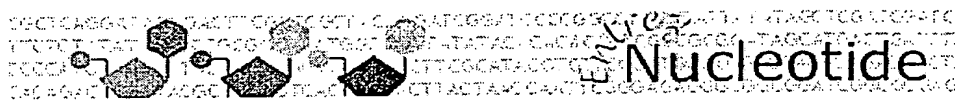
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Links

LOCUS PDGFC 3007 bp mRNA linear PRI 17-AUG-2001
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 REFERENCE 1 (bases 1 to 3007)
 AUTHORS Li,X., Ponten,A., Aase,K., Karlsson,L., Abramsson,A., Uutela,M.,
 Backstrom,G., Hellstrom,M., Bostrom,H., Li,H., Soriano,P.,
 Betsholtz,C., Heldin,C.H., Alitalo,K., Ostman,A. and Eriksson,U.
 TITLE PDGF-C is a new protease-activated ligand for the PDGF
 alpha-receptor
 JOURNAL Nat. Cell Biol. 2 (5), 302-309 (2000)
 MEDLINE 20268201
 PUBMED 10806482
 REFERENCE 2 (bases 1 to 3007)
 AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.
 TITLE A novel gene derived from developing spinal cords, SCDGF, is a
 unique member of the PDGF/VEGF family
 JOURNAL FEBS Lett. 475 (2), 97-102 (2000)
 MEDLINE 20317014
 PUBMED 10858496
 REFERENCE 3 (bases 1 to 3007)
 AUTHORS Tsai,Y.J., Lee,R.K., Lin,S.P. and Chen,Y.H.
 TITLE Identification of a novel platelet-derived growth factor-like gene,
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 JOURNAL Biochim. Biophys. Acta 1492 (1), 196-202 (2000)
 MEDLINE 20461776
 PUBMED 11004490
 REFERENCE 4 (bases 1 to 3007)
 AUTHORS Zwerner,J.P. and May,W.A.
 TITLE PDGF-C is an EWS/FLI induced transforming growth factor in Ewing
 family tumors
 JOURNAL Oncogene 20 (5), 626-633 (2001)
 MEDLINE 21214457
 PUBMED 11313995
 REFERENCE 5 (bases 1 to 3007)
 AUTHORS Uutela,M., Lauren,J., Bergsten,E., Li,X., Horelli-Kuitunen,N.,
 Eriksson,U. and Alitalo,K.
 TITLE Chromosomal location, exon structure, and vascular expression
 patterns of the human PDGFC and PDGFC genes
 JOURNAL Circulation 103 (18), 2242-2247 (2001)
 MEDLINE 21266739
 PUBMED 11342471

REFERENCE 6 (bases 1 to 3007)

AUTHORS Gilbertson,D.G., Duff,M.E., West,J.W., Kelly,J.D., Sheppard,P.O., Hofstrand,P.D., Gao,Z., Shoemaker,K., Bukowski,T.R., Moore,M., Feldhaus,A.L., Humes,J.M., Palmer,T.E. and Hart,C.E.

TITLE Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor

JOURNAL J. Biol. Chem. 276 (29), 27406-27414 (2001)

MEDLINE 21347863

PUBMED 11297552

COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [AF091434.1](#).
Summary: The protein encoded by this gene is a member of the platelet-derived growth factor family. The four members of this family are mitogenic factors for cells of mesenchymal origin and are characterized by a core motif of eight cysteines. This gene product appears to form only homodimers. It differs from the platelet-derived growth factor alpha and beta polypeptides in having an unusual N-terminal domain, the CUB domain.
COMPLETENESS: full length.

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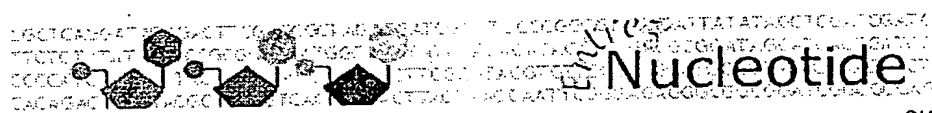
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Search for

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 JOURNAL J. Biol. Chem. 276 (29), 27406-27414 (2001)
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 AUTHORS Gao,Z., Hart,C., Piddington,C., Sheppard,P., Shoemaker,K., Gilbertson,D., West,J. and O'Hara,P.J.
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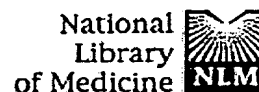
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Revised: July 5, 2002.

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PubMed Central

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☐ 1: Biochim Biophys Acta 2000 Jun 21;1492(1):196-202

Related Articles, Link

**ELSEVIER SCIENCE
FULL-TEXT ARTICLE****Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract.****Tsai YJ, Lee RK, Lin SP, Chen YH.**

Division of Reproduction and Endocrinolgy, Department of Medical Research, Mackay Memorial Hospital, Tamshui, Taiwan.
yjtsai@ms1.mmh.org.tw

We isolated the cDNA of a novel platelet-derived growth factor-like gene from human endometrium. The gene was named fallotein; it was 3007 bases in length, and encoded a protein of 345 amino acids. Antiserum against the fallotein protein can recognize a specific protein in the fallopian tube, with a molecular size in accordance with the anticipated size of fallotein. Fallotein mRNA is expressed in two molecular sizes, 3.8 and 2.9 kb, with the former being more abundant. High expression of the gene was found in the prostate, testis, and uterus. A weaker expression signal was found in the spleen, thymus, and small intestine, but expression of fallotein in the colon and peripheral blood leukocytes was negligible.

PMID: 11004490 [PubMed - indexed for MEDLINE]

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Mar 3 2003 10:01:4

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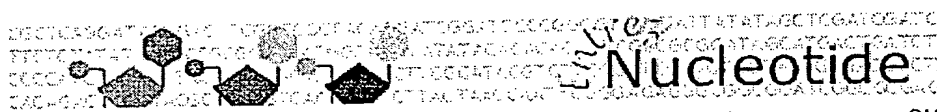
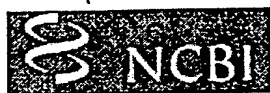
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Links

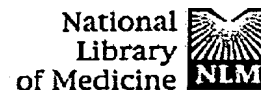
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REFERENCE 1 (bases 1 to 3007)
AUTHORS Tsai,Y.J., Lee,R.K., Lin,S.P. and Chen,Y.H.
TITLE Identification of a novel platelet-derived growth factor-like gene,
fallotein, in the human reproductive tract
JOURNAL Biochim. Biophys. Acta 1492 (1), 196-202 (2000)
MEDLINE 20461776
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AUTHORS Tsai,Y.J., Lee,R.K.K. and Lin,S.P.
TITLE Direct Submission
JOURNAL Submitted (14-SEP-1998) Dept. Medical Research, Mackay Memorial
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1: FEBS Lett 2000 Jun 16;475(2):97-102

Related Articles, Link

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/VEGF family.

Hamada T, Ui-Tei K, Miyata Y.

Department of Pharmacology, Nippon Medical School, Tokyo, Japan.

We isolated a novel gene designated spinal cord-derived growth factor (SCDGF). Its expression was increased in chick spinal cords with embryonic development and decreased after hatching. The amino acid sequences of chick and human SCDGFs revealed a putative signal sequence followed by a CUB domain and a region homologous to the members of the platelet-derived growth factor/vascular endothelial growth factor family. Furthermore, human SCDGF secreted from the cells showed a mitogenic activity for 10T1/2 cells in vitro. These results led us to speculate that SCDGF plays an important role in the development of the spinal cord.

PMID: 10858496 [PubMed - indexed for MEDLINE]

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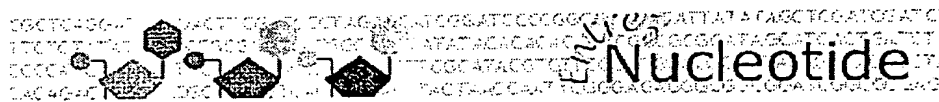
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☐ 1: AB033831. Homo sapiens hSCD...[gi:9392293]

Links

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DEFINITION Homo sapiens hSCDGF mRNA for spinal cord-derived growth factor,
complete cds.

ACCESSION AB033831

VERSION AB033831.1 GI:9392293

KEYWORDS spinal cord-derived growth factor; scdgm gene.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (sites)

AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.

TITLE A novel gene derived from developing spinal cords, SCDGF, is a
unique member of the PDGF/VEGF family

JOURNAL FEBS Lett. 475 (2), 97-102 (2000)

MEDLINE 20317014

PUBMED 10858496

REFERENCE 2 (bases 1 to 1817)

AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.

TITLE Direct Submission

JOURNAL Submitted (25-OCT-1999) Tsuyoshi Hamada, Nippon Medical School,
Department of Pharmacology; 1-1-5, Sendagi, Bunkyo-ku, Tokyo
113-8602, Japan (E-mail:t-hamada@nms.ac.jp,
Tel:81-3-3822-2131(ex.5277), Fax:81-3-5814-1684)

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1021 aatccagagt ggtggatctg aaccttctaa cagaggaggt aagattatac agctgcacac
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1501 attctgaaag aggagacatc aaacagaatt aggagttgtg caacagctct tttgagagga
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1741 agtgatcacc tgattccgtt gccttgctta actctaaagc tccatgtcct gggcctaaaa
1801 tcgtataaaa tctggat
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//

Revised: July 5, 2002.

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Mar 3 2003 10:13:39

Query= SEQ ID NO:6
 (918 letters)

Sequences producing significant alignments:

Score E
 (bits) Value

AC092608.2.1.196952 430 e-118
 AC093325.3.1.130754 236 2e-59

>AC092608.2.1.196952
 Length = 196952

Score = 430 bits (217), Expect = e-118
 Identities = 217/217 (100%)
 Strand = Plus / Minus

Query: 702 aggagataattatgaaaaggaaaaaaatctgaagaccaacttttacaaatatttggcaga 761
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 Sbjct: 74905 aggagataattatgaaaaggaaaaaaatctgaagaccaacttttacaaatatttggcaga 74846

Query: 762 gggaaacttctttaatattattatagttaagctattcaaaaagtatcctttggtacatta 821
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Sbjct: 74845 gggaaacttctttaatattattatagttaagctattcaaaaagtatcctttggtacatta 74786

Query: 822 tctttctttcttcttttcttttcttctttatttgccttcccccccaaaagtactatac 881
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 Sbjct: 74785 tctttctttcttcttttcttttcttctttatttgccttcccccccaaaagtactatac 74726

Query: 882 aatgtttcaagaatgtatgacatatgacttaacttaa 918
 ||||||||||||||||||||||||||||||||||||
 Sbjct: 74725 aatgtttcaagaatgtatgacatatgacttaacttaa 74689

Score = 414 bits (209), Expect = e-113
 Identities = 209/209 (100%)
 Strand = Plus / Minus

Query: 496 caattcacagaagctgtgagtccttcagtgctaccccccttcagctttgccactggacctg 555
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Sbjct: 77153 caattcacagaagctgtgagtccttcagtgctaccccccttcagctttgccactggacctg 77094

Query: 556 cttaataatgctataactgccttttagtaccttggagaccttattcgatatcttgaacca 615
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Sbjct: 77093 cttaataatgctataactgccttttagtaccttggagaccttattcgatatcttgaacca 77034

Query: 616 gagagatggcagttggacttagaagatctatataggccaacttggcaacttcttggcaag 675
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 Sbjct: 77033 gagagatggcagttggacttagaagatctatataggccaacttggcaacttcttggcaag 76974

Query: 676 gcttttggttttgaagaaaatccagagg 704
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Sbjct: 76973 gcttttggttttgaagaaaatccagagg 76945

Score = 396 bits (200), Expect = e-108
Identities = 200/200 (100%)
Strand = Plus / Minus

Query: 118 ggagtacaagatcctcagcatgagagaattattactgtgtctactaatggaagtattcac 177
|||||
Sbjct: 154677 ggagtacaagatcctcagcatgagagaattattactgtgtctactaatggaagtattcac 154618

Query: 178 agcccaagggtttcctcatacttatccaagaaatacgggtcttggtatggagattagtagca 237
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Sbjct: 154617 agcccaagggtttcctcatacttatccaagaaatacgggtcttggtatggagattagtagca 154558

Query: 238 gtagaggaaaatgtatggatacaacttacgtttgatgaaagatttgggcttgaagaccca 297
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Sbjct: 154557 gtagaggaaaatgtatggatacaacttacgtttgatgaaagatttgggcttgaagaccca 154498

Query: 298 gaagatgacatatgcaagta 317
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Sbjct: 154497 gaagatgacatatgcaagta 154478

Score = 361 bits (182), Expect = 5e-97
Identities = 185/186 (99%)
Strand = Plus / Minus

Query: 310 tgcaagtatgattttgtagaagttgaggaacccagtgatggaactatattagggcgctgg 369
|||||
Sbjct: 115282 tgcaggtatgattttgtagaagttgaggaacccagtgatggaactatattagggcgctgg 115223

Query: 370 tgtggttctggtactgtaccaggaaaacagattttctaaaggaaatcaaattaggataaga 429
|||||
Sbjct: 115222 tgtggttctggtactgtaccaggaaaacagattttctaaaggaaatcaaattaggataaga 115163

Query: 430 tttgtatctgatgaatattttccttctgaaccagggttctgcacccactacaacattgtc 489
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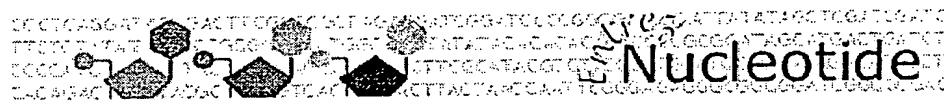
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Sbjct: 115102 atgcca 115097

>AC093325.3.1.130754
Length = 130754

Score = 236 bits (119), Expect = 2e-59
Identities = 119/119 (100%)
Strand = Plus / Minus

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|||||
Sbjct: 80211 atgagcctcttcgggcttctcctgctgacatctgccctggccggccagagacaggggact 80152

Query: 61 caggcggaatccaacctgagtagtaaattccagttttccagcaacaaggaacagaacgg 119
|||||
Sbjct: 80151 caggcggaatccaacctgagtagtaaattccagttttccagcaacaaggaacagaacgg 80093



PubMed

Nucleotide

Protein

Genome

Structure

PMC

Taxonomy

OMIM

Boo

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History

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Details

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Show:

Send to

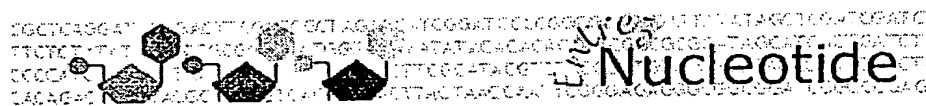
File

Get Subsequence

☐ 1: AC092608. Homo sapiens BAC ...[gi:15668121]

Links

LOCUS AC092608 196952 bp DNA linear PRI 01-MAR-2002
 DEFINITION Homo sapiens BAC clone RP11-154F14 from 4, complete sequence.
 ACCESSION AC092608 AC009582
 VERSION AC092608.2 GI:15668121
 KEYWORDS HTG.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 196952)
 AUTHORS Sulston, J.E. and Waterston, R.
 TITLE Toward a complete human genome sequence
 JOURNAL Genome Res. 8 (11), 1097-1108 (1998)
 MEDLINE 99063792
 PUBMED 9847074
 REFERENCE 2 (bases 1 to 196952)
 AUTHORS Isak, A., Kozlowicz, A. and Hawkins, M.
 TITLE The sequence of Homo sapiens BAC clone RP11-154F14
 JOURNAL Unpublished (2001)
 REFERENCE 3 (bases 1 to 196952)
 AUTHORS Waterston, R.H.
 TITLE Direct Submission
 JOURNAL Submitted (19-JUL-2001) Genome Sequencing Center, Washington
 University School of Medicine, 4444 Forest Park Parkway, St. Louis,
 MO 63108, USA
 REFERENCE 4 (bases 1 to 196952)
 AUTHORS Waterston, R.H.
 TITLE Direct Submission
 JOURNAL Submitted (19-SEP-2001) Genome Sequencing Center, Washington
 University School of Medicine, 4444 Forest Park Parkway, St. Louis,
 MO 63108, USA
 REFERENCE 5 (bases 1 to 196952)
 AUTHORS Waterston, R.
 TITLE Direct Submission
 JOURNAL Submitted (01-MAR-2002) Department of Genetics, Washington
 University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA
 COMMENT On Sep 19, 2001 this sequence version replaced gi:14916193.
 ----- Genome Center
 Center: Washington University Genome Sequencing Center
 Center code: WUGSC
 Web site: <http://genome.wustl.edu/gsc>
 Contact: sapiens@watson.wustl.edu
 ----- Summary Statistics
 Center project name: H_NH0154F14
 Drafting Center: WIBR



Search for

☐ 1: AC093325. Homo sapiens BAC ...[gi:15982602]

Links

LOCUS AC093325 130754 bp DNA linear PRI 09-JAN-2002
 DEFINITION Homo sapiens BAC clone RP11-612J15 from 4, complete sequence.
 ACCESSION AC093325
 VERSION AC093325.3 GI:15982602
 KEYWORDS HTG.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 130754)
 AUTHORS Sulston, J.E. and Waterston, R.
 TITLE Toward a complete human genome sequence
 JOURNAL Genome Res. 8 (11), 1097-1108 (1998)
 MEDLINE 99063792
 PUBMED 9847074

REFERENCE 2 (bases 1 to 130754)
 AUTHORS Waligorski, J. and Haakenson, W.
 TITLE The sequence of Homo sapiens BAC clone RP11-612J15
 JOURNAL Unpublished (2002)

REFERENCE 3 (bases 1 to 130754)
 AUTHORS Waterston, R.H.
 TITLE Direct Submission
 JOURNAL Submitted (18-AUG-2001) Genome Sequencing Center, Washington
 University School of Medicine, 4444 Forest Park Parkway, St. Louis,
 MO 63108, USA

REFERENCE 4 (bases 1 to 130754)
 AUTHORS Waterston, R.H.
 TITLE Direct Submission
 JOURNAL Submitted (07-OCT-2001) Genome Sequencing Center, Washington
 University School of Medicine, 4444 Forest Park Parkway, St. Louis,
 MO 63108, USA

REFERENCE 5 (bases 1 to 130754)
 AUTHORS Waterston, R.
 TITLE Direct Submission
 JOURNAL Submitted (09-JAN-2002) Department of Genetics, Washington
 University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Oct 7, 2001 this sequence version replaced gi:15624997.
 ----- Genome Center
 Center: Washington University Genome Sequencing Center
 Center code: WUGSC
 Web site: <http://genome.wustl.edu/gsc>
 Contact: sapiens@watson.wustl.edu
 ----- Summary Statistics
 Center project name: H_NH0612J15

NOTICE: This sequence may not represent the entire insert of this